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Figure 1Structure of V_H domain of human A6 antibody.

1	2	3	4	5	6	7	8	9	10	11	12	13	14
GAG	GTC	CAG	CTG	CAG	GAG	TCT	GGG	GGA	GGC	TTA	GTC	CAG	CCT
E	V	Q	L	Q	E	S	G	G	G	L	V	Q	P
15	16	17	18	19	20	21	22	23	24	25	26	27	28
GGG	GGG	TCC	CTG	AGA	CTC	TCC	TGT	TCA	GCC	TCT	GGA	TTC	ACC
G	G	S	L	R	L	S	C	S	A	S	G	F	T
29	30	31	32	33	34	35	36	37	38	39	40	41	42
TTC	AGT	AGC	TAT	GCT	ATG	CAC	TGG	GTC	CGC	CAG	GCT	CCA	GGG
F	S	<u>S</u>	<u>Y</u>	<u>A</u>	<u>M</u>	<u>H</u>	W	V	R	Q	A	P	G
CDR1													
43	44	45	46	47	48	49	50	51	52	a	53	54	55
AAG	GGA	CTG	GAA	TAT	GTT	TCA	GCT	ATT	AGT	AGT	AAT	GGG	GGT
K	G	L	E	Y	V	S	<u>A</u>	<u>I</u>	<u>S</u>	<u>S</u>	<u>N</u>	<u>G</u>	<u>G</u>
CDR2													
56	57	58	59	60	61	62	63	64	65	66	67	68	69
AGC	ACA	TAC	TAC	GCA	GAC	TCC	GTG	AAG	GGC	AGA	TTC	ACC	ATC
<u>S</u>	<u>T</u>	<u>Y</u>	<u>Y</u>	<u>A</u>	<u>D</u>	<u>S</u>	<u>V</u>	<u>K</u>	<u>G</u>	R	F	T	I
70	71	72	73	74	75	76	77	78	79	80	81	82	a
TCC	AGA	GAC	AAT	TCC	AAG	AAC	ACT	CTG	TAT	CTT	CAA	ATG	AGC
S	R	D	N	S	K	N	T	L	Y	L	Q	M	S
b	c	83	84	85	86	87	88	89	90	91	92	93	94
AGT	CTG	AGA	GCT	GAG	GAC	ACG	GCT	GTG	TAT	TAC	TGT	GTG	AAA
S	L	R	A	E	D	T	A	V	Y	Y	C	V	K

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Figure 1 (continued)

95	96	97	98	99	100	a	b	c	d	e	f	g	h
GAC	AGG	TTA	AAA	GTG	GAG	TAC	TAT	GAT	AGT	AGT	GGT	TAT	TAC
D	R	L	K	V	E	Y	Y	D	S	S	G	Y	Y

CDR3

i	j	k	l	m	n	o	101	102	103	104	105	105	107
GTT	TCT	CGG	TTC	GGT	GCT	TTT	GAT	ATC	TGG	GGC	CAA	GGG	ACA
V	S	R	F	G	A	F	D	I	W	G	Q	G	T

108	109	110	111	112	113
ACG	GTC	ACC	GTC	TCA	TCA
T	V	T	V	S	S

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Figure 2

Structure of modified V_H domain of human A6 antibody showing substitutions at position 44, 45, 47, 93 and 94. The NheI site is underlined.

1	2	3	4	5	6	7	8	9	10	11	12	13	14
GAG	GTC	CAG	CTG	CAG	GAG	TCT	GGG	GGA	GGC	TTA	GTC	CAG	CCT
E	V	Q	L	Q	E	S	G	G	G	L	V	Q	P
15	16	17	18	19	20	21	22	23	24	25	26	27	28
GGG	GGG	TCC	CTG	AGA	CTC	TCC	TGT	TCA	<u>GCT</u>	<u>AGC</u>	GGA	TTC	ACC
G	G	S	L	R	L	S	C	S	A	S	G	F	T
29	30	31	32	33	34	35	36	37	38	39	40	41	42
TTC	AGT	AGC	TAT	GCT	ATG	CAC	TGG	GTC	CGC	CAG	GCT	CCA	GGG
F	S	<u>S</u>	<u>Y</u>	<u>A</u>	<u>M</u>	<u>H</u>	W	V	R	Q	A	P	G
CDR1													
43	44	45	46	47	48	49	50	51	52	a	53	54	55
AAG	GAA	CGT	GAA	GGT	GTT	TCA	GCT	ATT	AGT	AGT	AAT	GGG	GGT
K	E	R	E	G	V	S	<u>A</u>	<u>I</u>	<u>S</u>	<u>S</u>	<u>N</u>	<u>G</u>	<u>G</u>
CDR2													
56	57	58	59	60	61	62	63	64	65	66	67	68	69
AGC	ACA	TAC	TAC	GCA	GAC	TCC	GTG	AAG	GGC	AGA	TTC	ACC	ATC
<u>S</u>	<u>T</u>	<u>Y</u>	<u>Y</u>	<u>A</u>	<u>D</u>	<u>S</u>	<u>V</u>	<u>K</u>	<u>G</u>	R	F	T	I
70	71	72	73	74	75	76	77	78	79	80	81	82	a
TCC	AGA	GAC	AAT	TCC	AAG	AAC	ACT	CTG	TAT	CTT	CAA	ATG	AGC
S	R	D	N	S	K	N	T	L	Y	L	Q	M	S
b	c	83	84	85	86	87	88	89	90	91	92	93	94
AGT	CTG	AGA	GCT	GAG	GAC	ACG	GCT	GTG	TAT	TAC	TGT	GCA	GCA
S	L	R	A	E	D	T	A	V	Y	Y	C	A	A

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Figure 2 (continued)

95	96	97	98	99	100	a	b	c	d	e	f	g	h
GAC	AGG	TTA	AAA	GTG	GAG	TAC	TAT	GAT	AGT	AGT	GGT	TAT	TAC
D	R	L	K	V	E	Y	Y	D	S	S	G	Y	Y

CDR3

i	j	k	l	m	n	o	101	102	103	104	105	105	107
GTT	TCT	CGG	TTC	GGT	GCT	TTT	GAT	ATC	TGG	GGC	CAA	GGG	ACA
V	S	R	F	G	A	F	D	I	W	G	Q	G	T

108	109	110	111	112	113
ACG	GTC	ACC	GTC	TCA	TCA
T	V	T	V	S	S

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Figure 3

Structure of V_H domain of human A6 antibody. The mutated nucleotides spanning residues 7-48 to remove the recombination site are in bold and underlined.

1	2	3	4	5	6	7	8	9	10	11	12	13	14
GAG	GTC	<u>CAA</u>	<u>TTA</u>	<u>CAG</u>	<u>GAA</u>	<u>AGT</u>	<u>GGT</u>	<u>GGC</u>	<u>GGA</u>	<u>CTG</u>	<u>GTG</u>	<u>CAA</u>	<u>CCA</u>
E	V	Q	L	Q	E	S	G	G	G	L	V	Q	P

15	16	17	18	19	20	21	22	23	24	25	26	27	28
<u>GGA</u>	<u>GGA</u>	TCC	CTG	AGA	CTC	TCC	TGT	TCA	GCC	TCT	GGA	TTC	ACC
G	G	S	L	R	L	S	C	S	A	S	G	F	T

29	30	31	32	33	34	35	36	37	38	39	40	41	42
TTC	AGT	AGC	TAT	GCT	ATG	CAC	TGG	GTC	CGC	CAG	GCT	CCA	GGG
F	S	<u>S</u>	<u>Y</u>	<u>A</u>	<u>M</u>	<u>H</u>	W	V	R	Q	A	P	G

CDR1

43	44	45	46	47	48	49	50	51	52	a	53	54	55
AAG	GGA	CTG	GAA	TAT	GTT	TCA	GCT	ATT	AGT	AGT	AAT	GGG	GGT
K	G	L	E	Y	V	S	<u>A</u>	<u>I</u>	<u>S</u>	<u>S</u>	<u>N</u>	<u>G</u>	<u>G</u>

CDR2

56	57	58	59	60	61	62	63	64	65	66	67	68	69
AGC	ACA	TAC	TAC	GCA	GAC	TCC	GTG	AAG	GGC	AGA	TTC	ACC	ATC
<u>S</u>	<u>T</u>	<u>Y</u>	<u>Y</u>	<u>A</u>	<u>D</u>	<u>S</u>	<u>V</u>	<u>K</u>	<u>G</u>	R	F	T	I

70	71	72	73	74	75	76	77	78	79	80	81	82	a
TCC	AGA	GAC	AAT	TCC	AAG	AAC	ACT	CTG	TAT	CTT	CAA	ATG	AGC
S	R	D	N	S	K	N	T	L	Y	L	Q	M	S

b	c	83	84	85	86	87	88	89	90	91	92	93	94
AGT	CTG	AGA	GCT	GAG	GAC	ACG	GCT	GTG	TAT	TAC	TGT	GTG	AAA
S	L	R	A	E	D	T	A	V	Y	Y	C	V	K

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Figure 3 (continued)

95	96	97	98	99	100	a	b	c	d	e	f	g	h
GAC	AGG	TTA	AAA	GTG	GAG	TAC	TAT	GAT	AGT	AGT	GGT	TAT	TAC
D	R	L	K	V	E	Y	Y	D	S	S	G	Y	Y

CDR3

i	j	k	l	m	n	o	101	102	103	104	105	105	107
GTT	TCT	CGG	TTC	GGT	GCT	TTT	GAT	ATC	TGG	GGC	CAA	GGG	ACA
V	S	R	F	G	A	F	D	I	W	G	Q	G	T

108	109	110	111	112	113
ACG	GTC	ACC	GTC	TCA	TCA
T	V	T	V	S	S

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Figure 4

Structure of modified VH domain of human A6 antibody showing substitutions at position 44, 45, 47, 93 and 94. The mutated nucleotides spanning residues 7-48 to remove the recombination site as well as the *NheI* site are in bold and underlined.

1	2	3	4	5	6	7	8	9	10	11	12	13	14
GAG	GTC	<u>CAA</u>	<u>TTA</u>	<u>CAG</u>	<u>GAA</u>	<u>AGT</u>	<u>GGT</u>	<u>GGC</u>	<u>GGA</u>	<u>CTG</u>	<u>GTG</u>	<u>CAA</u>	<u>CCA</u>
E	V	Q	L	Q	E	S	G	G	G	L	V	Q	P
15	16	17	18	19	20	21	22	23	24	25	26	27	28
GGA	GGA	TCC	CTG	AGA	CTC	TCC	TGT	TCA	<u>GCT</u>	<u>AGC</u>	GGA	TTC	ACC
G	G	S	L	R	L	S	C	S	A	S	G	F	T
29	30	31	32	33	34	35	36	37	38	39	40	41	42
TTC	AGT	AGC	TAT	GCT	ATG	CAC	TGG	GTC	CGC	CAG	GCT	CCA	GGG
F	S	<u>S</u>	<u>Y</u>	<u>A</u>	<u>M</u>	<u>H</u>	W	V	R	Q	A	P	G
CDR1													
43	44	45	46	47	48	49	50	51	52	a	53	54	55
AAG	<u>GAA</u>	<u>CGT</u>	<u>GAA</u>	<u>GGT</u>	<u>GTT</u>	<u>TCA</u>	<u>GCT</u>	<u>ATT</u>	<u>AGT</u>	<u>AGT</u>	<u>AAT</u>	<u>GGG</u>	<u>GGT</u>
K	E	R	E	G	V	S	<u>A</u>	<u>I</u>	<u>S</u>	<u>S</u>	<u>N</u>	<u>G</u>	<u>G</u>
CDR2													
56	57	58	59	60	61	62	63	64	65	66	67	68	69
AGC	ACA	TAC	TAC	GCA	GAC	TCC	GTG	AAG	GGC	AGA	TTC	ACC	ATC
<u>S</u>	<u>T</u>	<u>Y</u>	<u>Y</u>	<u>A</u>	<u>D</u>	<u>S</u>	<u>V</u>	<u>K</u>	<u>G</u>	R	F	T	I
70	71	72	73	74	75	76	77	78	79	80	81	82	a
TCC	AGA	GAC	AAT	TCC	AAG	AAC	ACT	CTG	TAT	CTT	CAA	ATG	AGC
S	R	D	N	S	K	N	T	L	Y	L	Q	M	S

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Figure 4 (continued)

b	c	83	84	85	86	87	88	89	90	91	92	93	94
AGT	CTG	AGA	GCT	GAG	GAC	ACG	GCT	GTG	TAT	TAC	TGT	GCA	GCA
S	L	R	A	E	D	T	A	V	Y	Y	C	A	A

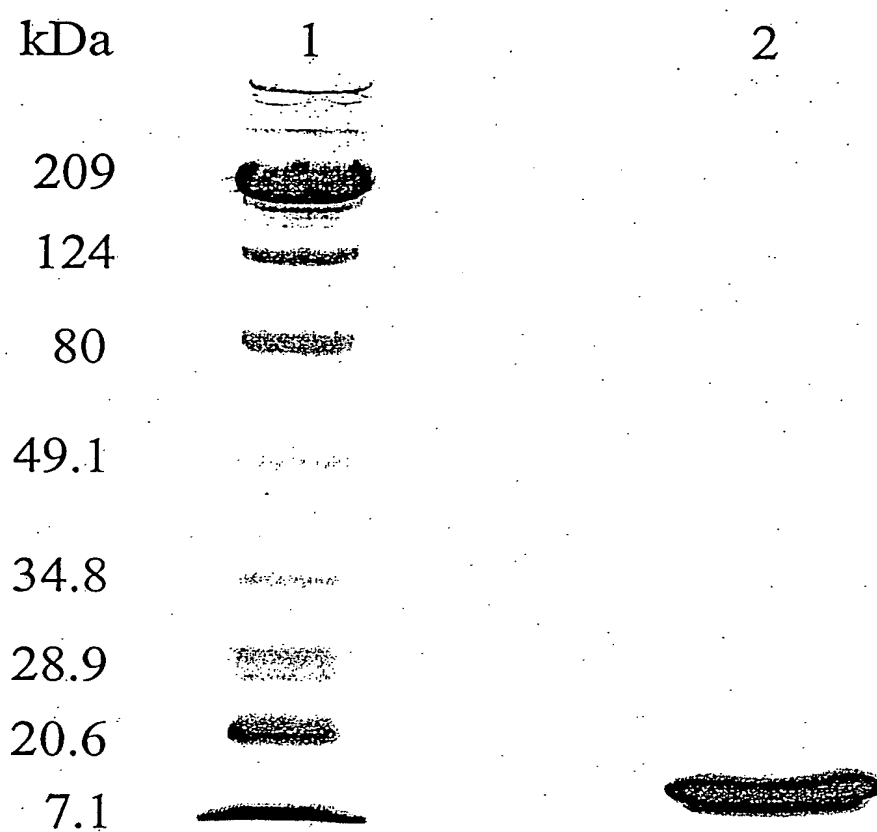
95	96	97	98	99	100	a	b	c	d	e	f	g	h
GAC	AGG	TTA	AAA	GTG	GAG	TAC	TAT	GAT	AGT	AGT	GGT	TAT	TAC
D	R	L	K	V	E	Y	Y	D	S	S	G	Y	Y

CDR3

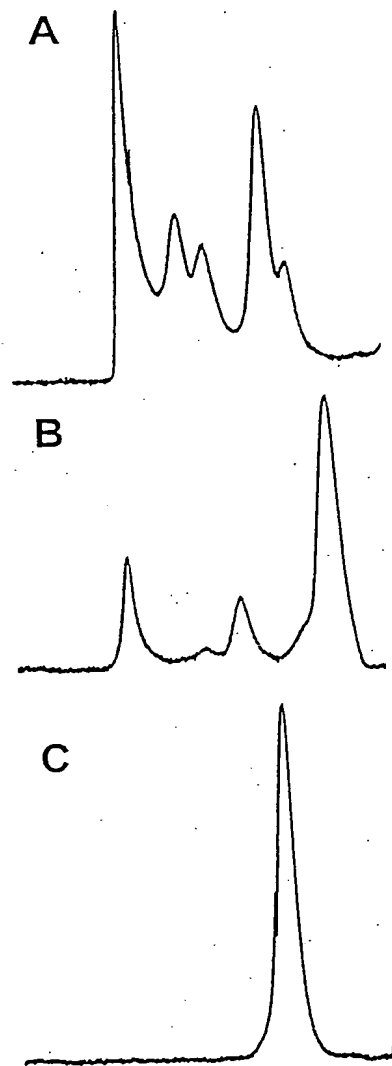
i	j	k	l	m	n	o	101	102	103	104	105	105	107
GTT	TCT	CGG	TTC	GGT	GCT	TTT	GAT	ATC	TGG	GGC	CAA	GGG	ACA
V	S	R	F	G	A	F	D	I	W	G	Q	G	T

108	109	110	111	112	113
ACG	GTC	ACC	GTC	TCA	TCA
T	V	T	V	S	S

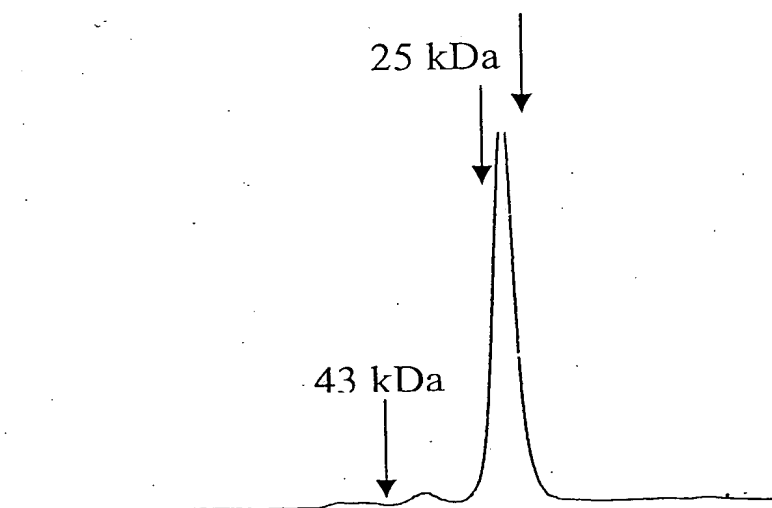
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Figure 5

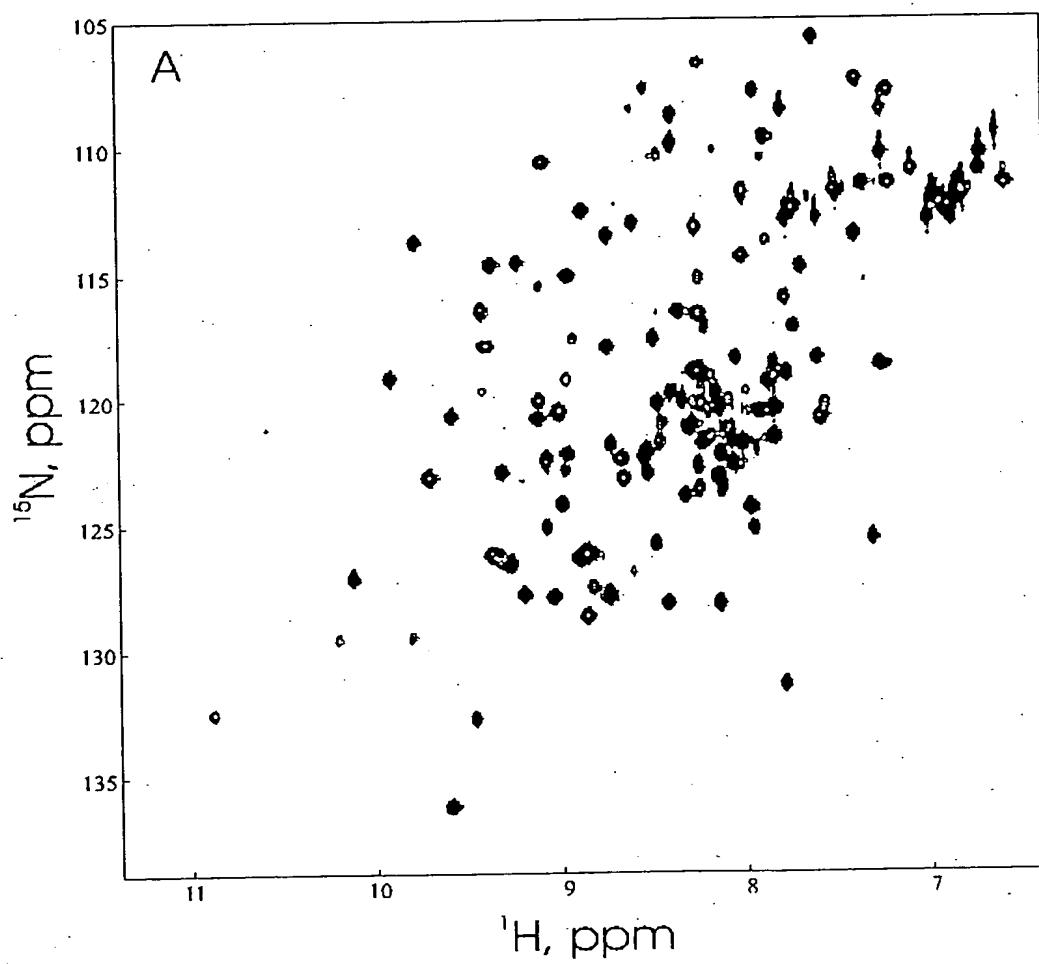
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Figure 6

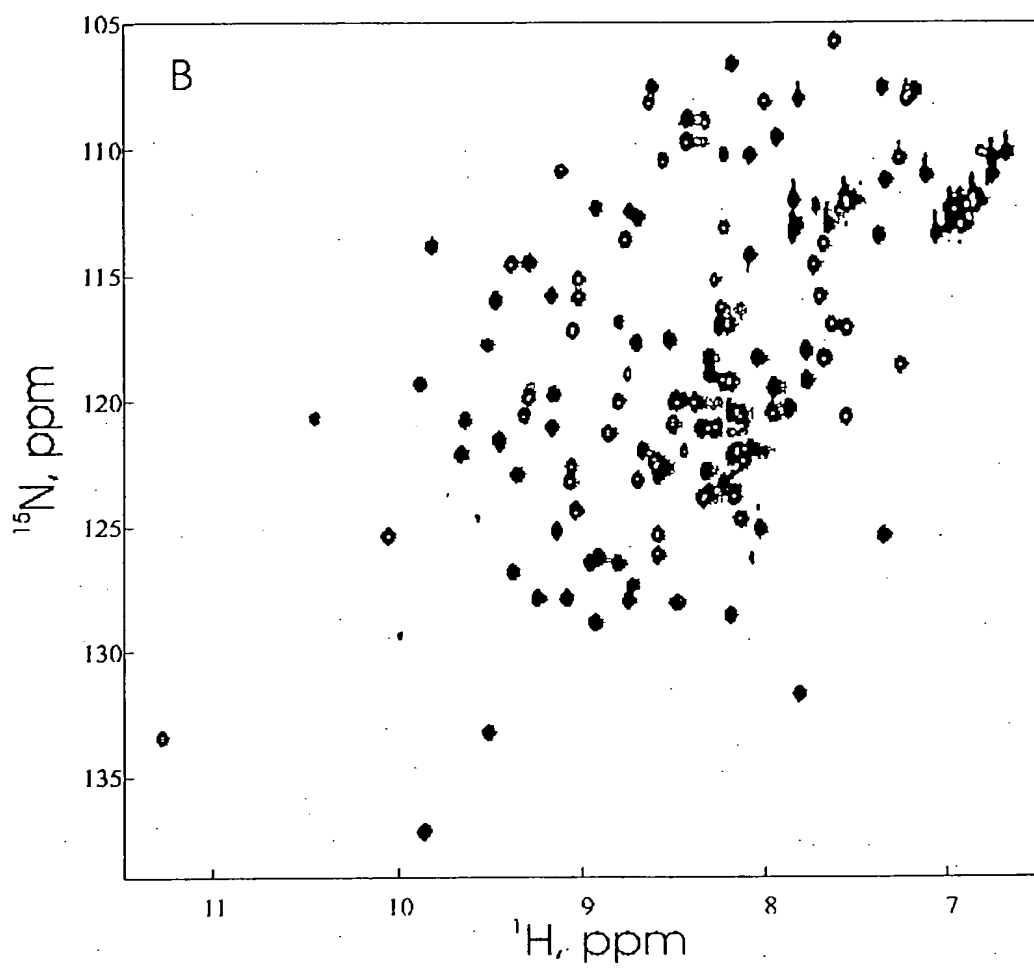
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Figure 7

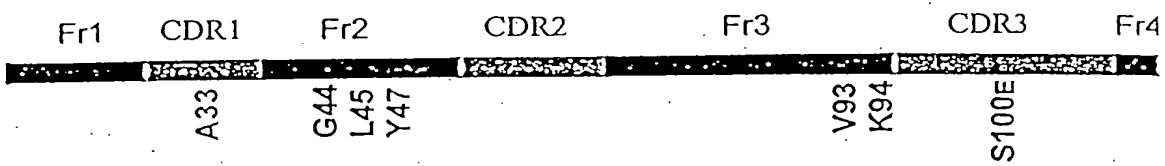
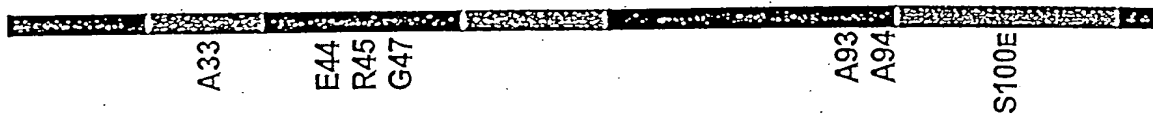
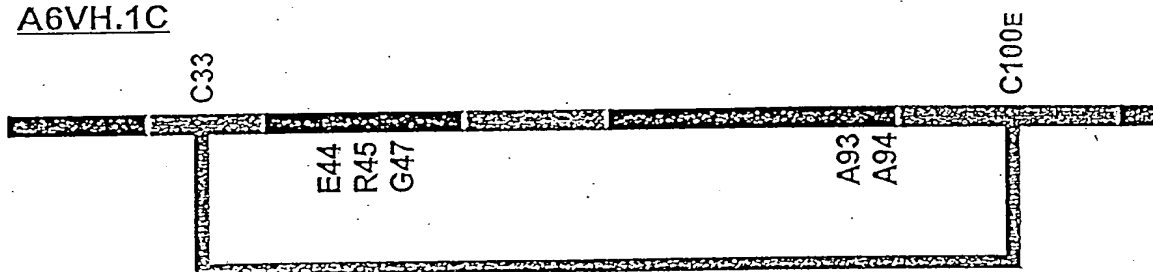
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Figure 8A

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Figure 8B

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Figure 9A6VHA6VH.1A6VH.1C

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Figure 10

Structure of modified V_H domain of human A6 antibody showing substitutions at position 33, 44, 45, 47, 93, 94 and 100e.

1	2	3	4	5	6	7	8	9	10	11	12	13	14
GAG	GTC	CAG	CTG	CAG	GAG	TCT	GGG	GGA	GGC	TTA	GTC	CAG	CCT
E	V	Q	L	Q	E	S	G	G	G	L	V	Q	P
15	16	17	18	19	20	21	22	23	24	25	26	27	28
GGG	GGG	TCC	CTG	AGA	CTC	TCC	TGT	TCA	GCC	TCT	GGA	TTC	ACC
G	G	S	L	R	L	S	C	S	A	S	G	F	T
29	30	31	32	33	34	35	36	37	38	39	40	41	42
TTC	AGT	AGC	TAT	<u>TGT</u>	ATG	CAC	TGG	GTC	CGC	CAG	GCT	CCA	GGG
F	S	<u>S</u>	<u>Y</u>	<u>C</u>	<u>M</u>	<u>H</u>	W	V	R	Q	A	P	G
CDR1													
43	44	45	46	47	48	49	50	51	52	a	53	54	55
AAG	<u>GAA</u>	<u>CGT</u>	GAA	GGT	GTT	TCA	GCT	ATT	AGT	AGT	AAT	GGG	GGT
K	<u>E</u>	<u>R</u>	E	G	V	S	<u>A</u>	<u>I</u>	<u>S</u>	<u>S</u>	N	G	G
CDR2													
56	57	58	59	60	61	62	63	64	65	66	67	68	69
AGC	ACA	TAC	TAC	GCA	GAC	TCC	GTG	<u>AAG</u>	GGC	AGA	TTC	ACC	ATC
<u>S</u>	<u>T</u>	<u>Y</u>	<u>Y</u>	<u>A</u>	<u>D</u>	<u>S</u>	<u>V</u>	<u>K</u>	<u>G</u>	R	F	T	I
70	71	72	73	74	75	76	77	78	79	80	81	82	a
TCC	AGA	GAC	AAT	TCC	AAG	AAC	ACT	CTG	TAT	CTT	CAA	ATG	AGC
S	R	D	N	S	K	N	T	L	Y	L	Q	M	S
b	c	83	84	85	86	87	88	89	90	91	92	93	94
AGT	CTG	AGA	GCT	GAG	GAC	ACG	GCT	GTG	TAT	TAC	TGT	<u>GCA</u>	<u>GCA</u>
S	L	R	A	E	D	T	A	V	Y	Y	C	A	A

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Figure 10 (continued)

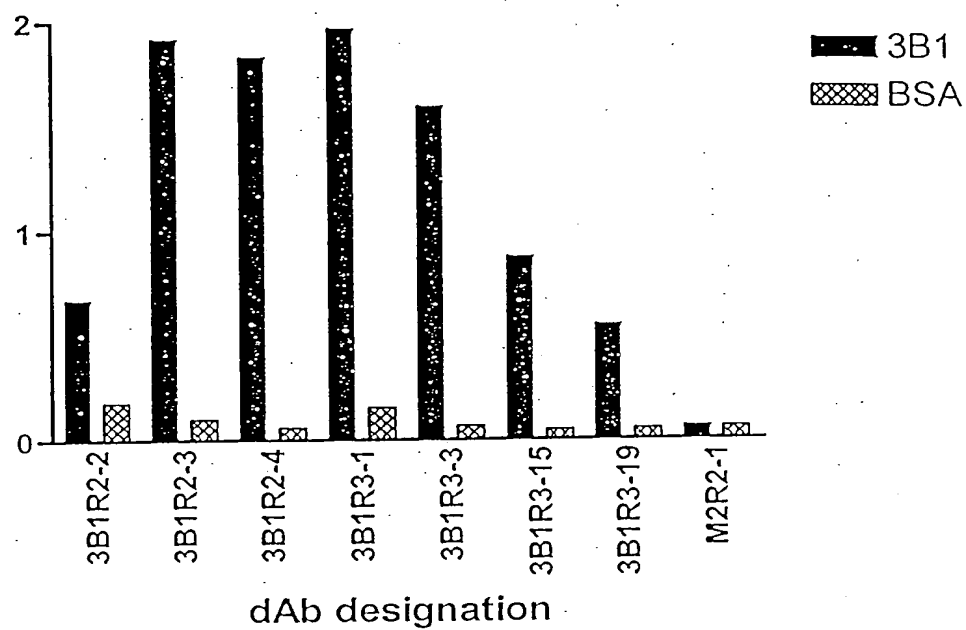
95	96	97	98	99	100	a	b	c	d	e	f	g	h
GAC	AGG	TTA	AAA	GTG	GAG	TAC	TAT	GAT	AGT	TGC	GGT	TAT	TAC
D	R	L	K	V	E	Y	Y	D	S	C	G	Y	Y

CDR3

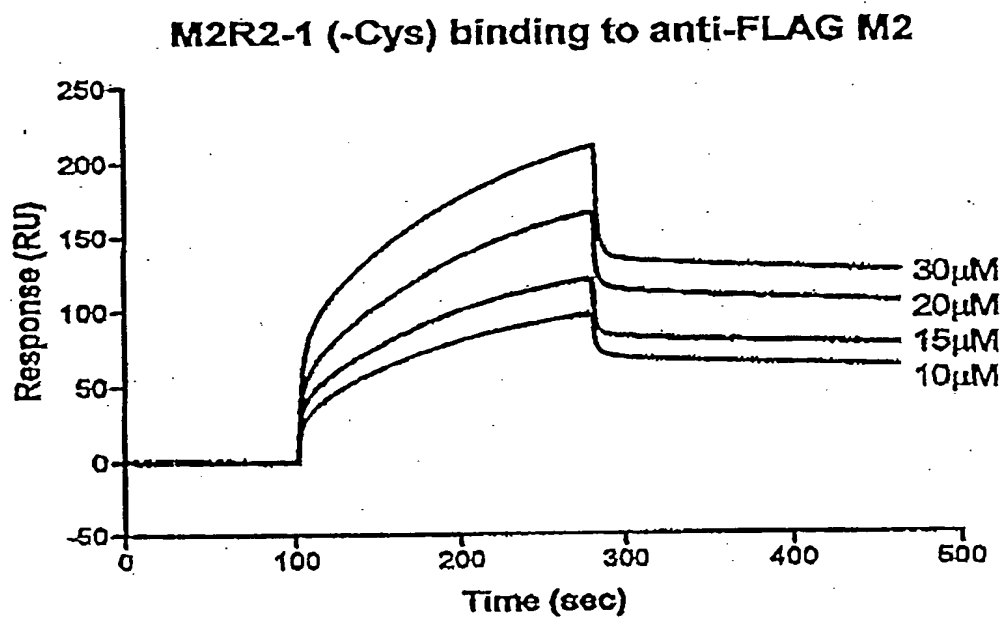
i	j	k	l	m	n	o	101	102	103	104	105	105	107
GTT	TCT	CGG	TTC	GGT	GCT	TTT	GAT	ATC	TGG	GGC	CAA	GGG	ACA
V	S	R	F	G	A	F	D	I	W	G	Q	G	T

108	109	110	111	112	113
ACG	GTC	ACC	GTC	TCA	TCA
T	V	T	V	S	S

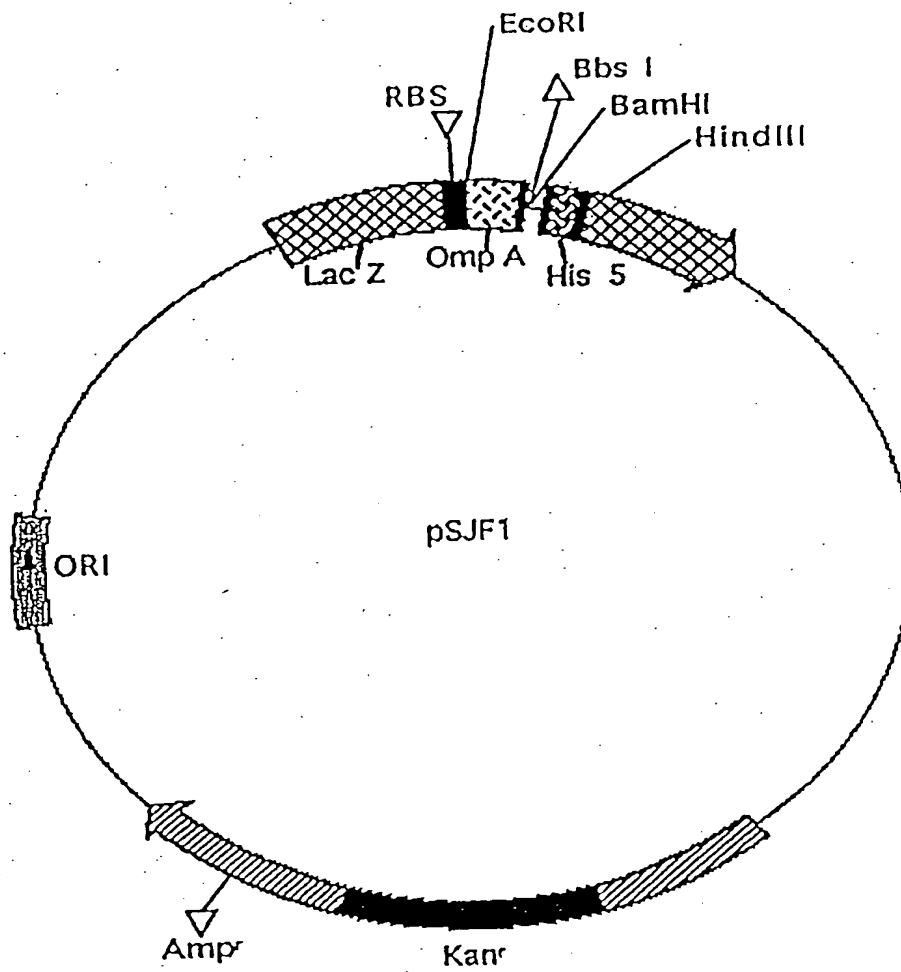
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Figure 11

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Figure 12

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Figure 13

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Figure 14

Structure of V_H domain of human A6 antibody. The mutated nucleotides spanning residues 7-48 to remove the recombination site are in bold and underlined.

1	2	3	4	5	6	7	8	9	10	11	12	13	14
GAG	GTC	<u>CAA</u>	<u>TTA</u>	<u>CAG</u>	<u>GAA</u>	<u>AGT</u>	<u>GGT</u>	<u>GGC</u>	<u>GGA</u>	<u>CTG</u>	<u>GTG</u>	<u>CAA</u>	<u>CCA</u>
E	V	Q	L	Q	E	S	G	G	G	L	V	Q	P

15	16	17	18	19	20	21	22	23	24	25	26	27	28
<u>GGA</u>	<u>GGA</u>	TCC	CTG	AGA	CTC	TCC	TGT	TCA	<u>GCT</u>	<u>AGC</u>	GGA	TTC	ACC
G	G	S	L	R	L	S	C	S	A	S	G	F	T

29	30	31	32	33	34	35	36	37	38	39	40	41	42
TTC	AGT	AGC	TAT	GCT	ATG	CAC	TGG	GTC	CGC	CAG	GCT	CCA	GGG
F	S	<u>S</u>	<u>Y</u>	<u>A</u>	<u>M</u>	<u>H</u>	W	V	R	Q	A	P	G

CDR1

43	44	45	46	47	48	49	50	51	52	a	53	54	55
AAG	GGA	CTG	GAA	TAT	GTT	TCA	GCT	ATT	AGT	AGT	AAT	GGG	GGT
K	G	L	E	Y	V	S	<u>A</u>	<u>I</u>	<u>S</u>	<u>S</u>	N	G	G

CDR2

56	57	58	59	60	61	62	63	64	65	66	67	68	69
AGC	ACA	TAC	TAC	GCA	GAC	TCC	GTG	AAG	GGC	AGA	TTC	ACC	ATC
<u>S</u>	<u>T</u>	<u>Y</u>	<u>Y</u>	<u>A</u>	<u>D</u>	<u>S</u>	<u>V</u>	<u>K</u>	<u>G</u>	R	F	T	I

70	71	72	73	74	75	76	77	78	79	80	81	82	a
TCC	AGA	GAC	AAT	TCC	AAG	AAC	ACT	CTG	TAT	CTT	CAA	ATG	AGC
S	R	D	N	S	K	N	T	L	Y	L	Q	M	S

b	c	83	84	85	86	87	88	89	90	91	92	93	94
AGT	CTG	AGA	GCT	GAG	GAC	ACG	GCT	GTG	TAT	TAC	TGT	GTG	AAA
S	L	R	A	E	D	T	A	V	Y	Y	C	V	K

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Figure 14 (continued)

95	96	97	98	99	100	a	b	c	d	e	f	g	h
GAC	AGG	TTA	AAA	GTG	GAG	TAC	TAT	GAT	AGT	AGT	GGT	TAT	TAC
D	R	L	K	V	E	Y	Y	D	S	S	G	Y	Y

CDR3

i	j	k	l	m	n	o	101	102	103	104	105	105	107
GTT	TCT	CGG	TTC	GGT	GCT	TTT	GAT	ATC	TGG	GGC	CAA	GGG	ACA
V	S	R	F	G	A	F	D	I	W	G	Q	G	T

108	109	110	111	112	113
ACG	GTC	ACC	GTC	TCA	TCA
T	V	T	V	S	S

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Figure 15